

## REMARKS

### *Present Invention*

The invention provides a method for producing a plant lipoxygenase (LOX) with modified positional specificity toward arachidonic acid and its use for hydroperoxylation of arachidonic acid. The LOX makes it possible to produce (11S,14Z,12E,8Z,5Z)-11-hydroperoxy-14,12,8,5-eicosatetraenic acids on a large scale.

### *Pending Claims*

Claims 12-28 are pending with claims 24-28 treated as withdrawn.

### *Amendment to the Claims*

Claim 12 has been amended to recite the EMBL database accession number of the potato tuber lipoxygenase amino acid sequence. This amendment is supported by the specification, for example, at page 4, lines 16-17. Accordingly, no new matter has been added by way of this amendment

### *Discussion of the Office Action*

Claims 12-23 stand rejected under Section 112, first and second paragraphs. Reconsideration of these rejections is hereby requested. In addition, the examination of claims 26 and 27 is requested.

### *Discussion of the Restrictions*

The Office set forth a Restriction Requirement in its Office Action dated March 11, 2004. In particular, the Office set forth the following groups of claims:

- (I) claims 12-17, 26, and 27, drawn to a method of modifying the specificity of a plant lipoxygenase, and the lipoxygenase protein,
- (II) claims 12-15 and 18-25, drawn to a method of modifying the specificity of a plant lipoxygenase and the DNA encoding the enzyme, vectors, cells, and plants, and
- (III) claim 28, drawn to arachidonic acid.

Applicants elected the claims of Group I and argued for joining the claims of Group II with the claims of Group I. The Office agreed. However, the Office Action has not considered claims 26 and 27 which the Office, in its Restriction Requirement, had included with the Group I claims. No reason is given why claims 26 and 27 were not examined.

Accordingly, it appears that the removal of claims 26 and 27 from examination was erroneous. Applicants request the examination of claims 26 and 27.

*Discussion of the Written Description Rejection*

Claims 12-23 have been rejected under 35 U.S.C. § 112, first paragraph, for an alleged lack of written description. Specifically, the Office Action alleges that the specification does not reasonably convey to the ordinarily skilled artisan that Applicants had possession of the claimed invention at the time the application was filed. The Office Action alleges that the claims are drawn to a genus of mutant lipoxxygenase but, by teaching only one representative species, the application has not described the whole genus. Applicants respectfully traverse the rejection.

One species can be enough to support a genus when it conveys to the ordinarily skilled artisan the necessary common attributes or features of elements possessed by the genus. This is especially true when the skill and knowledge in the art is high, as it is acknowledged to be in the biotechnological arts. (*See* January 5, 2001 Written Description Guidelines, 66 Fed. Reg. 1099, 1106.) The amino acid change, as claimed, is at position 576 of the lipoxxygenase of a potato tuber with the accession number S73865 or at the *corresponding position* of a lipoxxygenase in another plant species (claim 12, *see also* specification pages 3-4 & Table 1). The term “corresponding position” would be well understood by the ordinarily skilled artisan since the sequence motif GVLESTVFPSK is highly conserved in plant lipoxxygenases. Therefore, the specification teaches the common attributes or features of elements possessed by the genus.

Furthermore, more than one species are in fact taught. The “corresponding” amino acids relevant for the specificity of several plant lipoxxygenases (from two types of lipoxxygenases) have been determined by sequence comparisons and are shown in Table 1 on page 4. Such sequence comparisons are routinely performed in the art using various computer programs, and the teachings of Table 1 can readily be extended to other members of the genus. Accordingly, the ordinarily skilled artisan would recognize from the specification as filed that Applicants had possession of the claimed invention.

The Office Action further alleges that no evidence is on the record of a correlation between any plant lipoxxygenase comprising a mutation at the position 576 and an enhanced specificity towards position 11 of arachidonic acid. Claim 12 recites, as presently amended “at position 576 of potato tuber lipoxxygenase with the accession number S73865 in the EMBL database or at a corresponding position in a lipoxxygenase of another plant species.” As the specification teaches in Table 2 (specification page 10) mutation at position 576 of potato tuber

lipoxygenase markedly increases the specificity towards position 11 of arachidonic acid. The specification teaches that the amino acid sequence *corresponding* to the region around position 576 of potato tuber lipoxygenase is readily identified in other species of the genus by sequence comparison (*see, e.g.*, page 3, line 8, through page 4, line 19). The ordinarily skilled artisan would, therefore, recognize that the motif is well conserved in plant lipoxygenases and would also reasonable expect that mutations of the *corresponding* amino acids would have similar effect. The ordinarily skilled artisan would accordingly recognize that Applicants' disclosure of the potato tuber lipoxygenase mutation and the *corresponding* amino acids in other species represents possession of the claimed genus of plant lipoxygenase mutants. Applicants respectfully submit that the written description rejection is improper and request withdrawal of the written description rejection.

#### *Discussion of the Enablement Rejection*

The Office Action rejects claims 12-23 under 35 U.S.C. § 112, first paragraph, alleging that the specification is not enabling. Specifically, the Office Action alleges that the specification is only enabling for the 5-lipoxygenase mutant from potato tuber disclosed in the application. Applicants traverse this rejection for the reasons presented below.

The Office Action alleges that the application only discloses "a few lipoxgenases," and that the specification fails to provide guidance on how to isolate other lipoxygenases whose sequence is different from those disclosed in Table 1 on page 4. However, Table 1 on page 4 teaches seven different plant lipoxygenases from both the 15-LOX and 5-LOX lipoxygenase classes. Moreover, page 3 teaches that these were identified by sequence comparison with lipoxygenases in freely available sequence databases. In addition, the sequence motif GVLESTVFPSK, which can be used to screen such databases, is taught on page 4, line 11. Using this motif the ordinarily skilled artisan could readily identify other lipoxygenases in these data bases and use corresponding DNA sequences to isolate nucleic acids encoding these other lipoxygenases. In addition, the ordinarily skilled artisan could readily use amino sequences in any specific lipoxygenase corresponding to (*i.e.*, homologous to) the potato tuber GVLESTVFPSK motif to construct oligonucleotide probes with which to screen cDNA libraries of other plants to isolate the nucleic acids encoding other lipoxygenases. Thus, the present description, combined with the general knowledge in the field, provides sufficient guidance to isolate other lipoxygenases without undue experimentation.

The Office Action further alleges that there is a low level of predictability of the conservation of amino acids at the disclosed sequences in other lipoxygenases. This, the Office

Action contends, would result in screening beyond that which is routine in the art. As discussed above, however, the GVLESTVFPSK motif is well conserved, and screening would be focused on lipoxygenase sequences homologous to the motif. Accordingly, the amount of screening would only be routine.

In addition, even if inoperative embodiments within the scope of a claim are identified, this does not necessarily render a claim nonenabled. The standard is whether a skilled artisan could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art (M.P.E.P. § 2164.08(b)). In the present setting, the ordinarily skilled artisan could easily identify such inoperative lipoxygenases by the lack of an amino acid sequence with homology to the GVLESTVFPSK motif using a routine computer search.

Finally, the Office Action alleges that there is no evidence that mutating any plant lipoxygenase would result in enhanced specificity towards position 11 of arachidonic acid. The Office Action concludes that the ordinarily skilled artisan would require guidance in order to enhance the specificity of any plant lipoxygenase without undue experimentation. But, considerable guidance is provided by the specification of the present application. As the specification teaches in Table 2 (page 10), mutation at position 576 of potato tuber lipoxygenase markedly increases the specificity towards position 11 of arachidonic acid. The specification teaches that the amino acid sequence *corresponding* to the region around position 576 of potato tuber lipoxygenase is readily identified by sequence comparison (page 3, line 8, through page 4, line 19). The ordinarily skilled artisan can readily perform such sequence comparisons. The ordinarily skilled artisan would reasonably expect that mutation of the motif well conserved in plant lipoxygenases would have similar effects in other lipoxygenases. Similarly the type of amino acid changes that would produce the desired effect would be known to the ordinarily skilled artisan from the specification's teaching that a mutation to a phenylalanine is operative and the fact, well known in the art when the application was filed, that there are classes of amino acid changes which produce similar effects (*see, e.g.*, Voloshin et al., U.S. Patent No. 5,731,411, issued March 24, 1998). For the reasons stated herein, Applicants respectfully submit that the enablement rejection is improper and request the withdrawal of the enablement rejection.

#### *Discussion of the Indefiniteness Rejection*

The Office Action rejects claims 12-23 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the Office Action alleges that several lipoxygenase isoenzymes would exist in potato tuber and, thus, it would be unclear which residue would

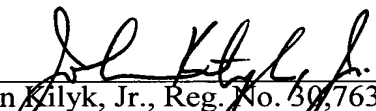
In re Appln. of Feussner et al.  
Application No. 10/030,464

correspond to "position 576." In an effort to advance prosecution of the subject application, and not in acquiescence of the rejection, claim 12 has been amended to include a recitation of the EMBL database accession number of the referenced amino acid sequence. As such the Section 112, second paragraph, rejection is rendered moot by this amendment.

*Conclusion*

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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